

CLAIMS

What is claimed is:

- 5        1. A method of detecting cancerous cells in a patient by detecting alterations of PP2C $\alpha$  gene activity in a specimen isolated from the patient.
- 10      2. The method of claim 1 wherein the specimen is selected from the group consisting of tissue biopsies and bodily fluids.
- 15      3. The method of claim 1 further characterized by the alteration being a reduction in PP2C $\alpha$  gene activity compared to normal controls.
- 20      4. The method of claim 1 wherein said detecting steps is further defined as assaying the specimen for mRNA complementary to PP2C $\alpha$  DNA including polymorphisms thereof with an assay selected from the group consisting of *in situ* hybridization, Northern blotting and reverse transcriptase - polymerase chain reaction.
- 25      5. The method of claim 1 wherein said detecting step is further defined as assaying the specimen for a PP2C $\alpha$  gene product including polymorphisms and peptide fragments thereof with an assay selected from the group consisting immunohistochemical and immunocytochemical staining, ELISA, RIA, immunoblots, immunoprecipitation, Western blotting, functional assays and protein truncation test.
- 30      6. The method of claim 5 wherein the specimen is bodily fluids selected from the group consisting of urine, blood, cerebralspinal fluid and saliva.

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7. The method of claim 1 wherein the detecting of PP2C $\alpha$  gene activity in a specimen is by determining alterations in phosphorylation patterns of proteins affected by the PP2C $\alpha$  gene product.

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8. A kit for detecting PP2C $\alpha$  activity as set forth in claim 4, said kit comprising:

a molecular probe complementary to genetic sequences of a mRNA for PP2C $\alpha$  including polymorphisms thereof and

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detection means for detecting hybridization of said molecular probe and the mRNA thereby indicating the activity of the PP2C $\alpha$  gene.

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9. A kit for detecting a gene product associated with PP2C gene activity as set forth in claim 5, said kit comprising:

an antibody which with high specificity recognizes markers selected from the group consisting of the PP2C $\alpha$  gene product including polymorphisms thereof and peptide fragments thereof, and

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detection means for detecting the binding of the antibody thereby indicating the presence of the gene product.

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10. A kit for detecting a gene product associated with PP2C gene activity as set forth in claim 5, said kit comprising:

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an agent which mimics natural proteins which bind to the PP2C $\alpha$  gene product including polymorphisms thereof and peptide fragments thereof, and

detection means for detecting the binding of the agent thereby indicating the presence of the gene product.

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11. A non-human transgenic mammal or cell line containing an expressible nucleic acid sequence for human PP2C $\alpha$  including polymorphisms thereof.

5 12. A non-human eucaryotic organism in which the equivalent genomic nucleic acid sequence for PP2C $\alpha$  is knocked-out.

10 13. A vector comprising an expression control sequence operatively linked to the nucleic acid sequence of PP2C $\alpha$ .

15 14. A host cell transformed with the vector of claim 13.

15 15. A vector comprising an antisense sequence of PP2C $\alpha$ .

20 16. An antibody which specifically binds to an epitope of a gene product of PP2C $\alpha$  including polymorphisms thereof which distinguishes the gene product of PP2C $\alpha$  from the gene product of PP2C $\beta$ .

25 17. An antibody of claim 16 conjugated to a detectable moiety.

18. An antibody of claim 16 selected from the group consisting of monoclonal and polyclonal antibody.

30 19. A polyclonal antibody of claim 18 raised against recombinantly produced PP2C $\alpha$ .

35 20. A polyclonal antibody of claim 18 raised against the carboxy terminal peptide of pp2c $\alpha$  selected from the group consisting of NDDTDSASTD (SEQ ID No:1) and ~~YKNDTDSTSTDDMW (SEQ ID No:2)~~.

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21. A monoclonal antibody of claim 18 which does not cross-react with pp2c $\beta$  and which is raised against peptides selected from the group consisting of recombinantly produced pp2c $\alpha$ , NDDTDSASTD (SEQ ID No:1) and YKNDDTDSTSTDDMW (SEQ ID No:2).

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22. A monoclonal antibody of claim 21 designated as 2A3.

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23. An isolated and purified peptide selected from the group consisting of NDDTDSASTD (SEQ ID No:1), YKNDDTDSTSTDDMW (SEQ ID No:2) and PNKDNDGGA (SEQ ID No:3).

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24. The peptide of claim 23 produced recombinantly.

25. A method of treating cancer including the steps of

20 a. determining the type of cancer and cells expressing the cancer,

b. preparing a vector which will specifically target the cancer cells including regulatory elements to control the expressibility of PP2C $\alpha$ , and

25 c. administering the vector to the patient.

26. The method as set forth in claim 25 wherein the vector includes an AAV modified sequence or part of the AAV sequence.

30 27. The method as set forth in claim 25 wherein the vector contains the CHINT sequences.

28. The method as set forth in claim 25 wherein 35 the vector includes the silencer region (SEQ ID No:13).

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29. The method as set forth in claim 25 wherein the vector includes the mini-silencer region (SEQ ID No:14).

5 30. A method of treating cancer including the steps of

a. determining the type of cancer and cells expressing the cancer,

10 b. preparing an antisense vector which will specifically target the cancer cells to control the expressibility of PP2C $\alpha$ , and

c. administering the vector to the patient.

15 31. A pharmaceutical composition consisting of a vector and a pharmaceutically suitable carrier wherein the vector is selected from the group consisting of a vector which will specifically target the cancer cells and including regulatory elements to control the expressibility of PP2C $\alpha$  and an antisense vector which 20 will specifically target the cancer cells to control the expressibility of PP2C $\alpha$ .

25 32. A method of treating diseases due to aberrant phosphorylation due to alteration of expression of PP2C $\alpha$  including

a. preparing an antisense vector which will specifically target cells expressing aberrant phosphorylation to control the expressibility of PP2C $\alpha$ , and

30 b. administering the vector to the patient.

35 33. A method of suppressing gene amplification by interrupting unscheduled interactions of DNA polymerase  $\alpha$  primase with the gene product of PP2C $\alpha$  by preparing an antisense vector which will specifically target the

binding region of DNA polymerase α primase to the PP2C $\alpha$  gene product and delivering the vector to the cells.

34. A method for the activation of the gene  
5 product of PP2C $\alpha$  expressed on the surface of a cell to induce signal transduction.

35. The method of claim 34 wherein an antibody is used to bind to the gene product of PP2C $\alpha$ .

10 36. A method of detecting cancer in a patient by detecting altered PP2C $\beta$  gene activity in a specimen isolated from the patient.

15 37. The method of claim 36 further characterized by detecting an increase in PP2C $\beta$  activity.

20 38. The method of claim 36 wherein the detecting of PP2C $\beta$  activity is by assaying the specimen for mRNA complementary to PP2C $\beta$  DNA including polymorphisms thereof with an assay selected from the group consisting of *in situ* hybridization, Northern blotting and reverse transcriptase - polymerase chain reaction.

25 39. The method of claim 36 wherein the detecting of PP2C $\beta$  activity is by assaying the specimen for a PP2C $\beta$  gene product including polymorphisms thereof with an assay selected from the group consisting immunohistochemical and immunocytochemical staining,  
30 ELISA, RIA, immunoblots, immunoprecipitation, Western blotting, functional assays and protein truncation test.

35 40. An antibody which specifically binds to an epitope of a gene product of PP2C $\beta$  including

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polymorphisms thereof which distinguishes the gene product of PP2C $\alpha$  from the gene product of PP2C $\beta$ .

5        41. An antibody of claim 40 conjugated to a detectable moiety.

10        42. An antibody of claim 40 selected from the group consisting of monoclonal and polyclonal antibody.

15        43. A polyclonal antibody of claim 40 raised against recombinantly produced PP2C $\beta$ .

20        44. A polyclonal antibody of claim 40 raised against the carboxy terminal peptide PNKDNDGGA (SEQ ID No:3)

